Journal of Applied Pharmaceutical Science
Available online at: https://japsonline.com

In silico screening and identification of lead molecules from *Garcinia gummi-gutta* with multitarget activity against SARS-CoV-2

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doi: https://doi.org/10.7324/JAPS.2024.150413

SUPPLEMENTARY MATERIAL

Supplementary Table 1: Interaction details of hit molecules with spike protein

Target protein	Phytochemicals	Binding energy(Kcal/mol)	Hydrogen bond	Bond length(A^0)	Hydrophobic interaction
Spike protein	1,4-Dicaffeoylquinic acid	-7.2	ILE410:O----H:Lig	2.63	THR376, LYS378
			TYR380:OH--H:Lig	2.46	
			GLY404:O----H:Lig	2.51	
			THR376:HG --H:Lig	2.46	
			ARG408:HE - O:Lig	2.79	
			ARG408:HH21--O:Lig	2.11	

			ASP405:CA --- O:Lig	3.55	
	Amentoflavone	-9	GLN493:OE1--N:Lig	3.69,4.03	ARG403
			GLN498:HE22--N:Lig	3.13	
			GLY502:HN--O:Lig	2.13	
			TYR505:O----H:Lig	1.83	
	Cambogic acid	-7.8	LEU517:O--H:Lig	1.84	LEU517, PRO426, PRO463, PRO426
			THR430:HG1--N:Lig	2.85	LEU517, LEU390, VAL382, PHE392,
			LEU517:HN--N:Lig	3.24	TYR396, PHE429, PHE464
	Dihydromorelloflavone	-7.3	ARG457:HH2 --O:Lig	2.46	ARG454, ARG457, LYS458,
			SER469:HG---O:Lig	2.36	ASP467, GLU471
			ARG466:O----H:Lig	2.47	
			GLU471:O----H:Lig	2.53	
	Luteolin 7-glucuronide	-7.7	:VAL407:O--H:Lig	2.23	ASP405, VAL407
			TYR380:OH--H:Lig	2.83	
			TYR508:HH - N:Lig:O	2.80	
	Morelloflavone	-8	GLU471:O--H:Lig	2.79	ARG457, ASP467, GLU471, LYS458
			SER469:HG --O:Lig	2.59	
	Oxyguttiferone K	-7.2	Nil		LYS378, TYR508, VAL433, ALA411
	Rheediaxanthone A	-7.5	TYR508:OH--H: Lig	2.39	ASP405, ARG408, VAL407
			ARG408:HH21-O:Lig	2.49	

Supplementary Table 2: Interaction details of hit molecules with ACE2

Target protein	Phytochemicals	Binding energy(Kcal/mol)	Hydrogen bond	Bond length(A^0)	Hydrophobic interaction
ACE2	1,4-Dicaffeoylquinic acid	-10.4	CYS344:HN--O:Lig	2.26	THR445, TYR127, LEU144, CYS344
			LYS363:HZ2--O:Lig	2.71	
			LYS363:HZ3--O:Lig	2.69	
			ASN149:OD1--H:Lig	2.06	
			GLU406:OE2--H:Lig	2.00	
	Amentoflavone	-11.6	ASP350:HN--O:Lig	2.39	HIS378,TYR510,
			ARG514:HH22-O:Lig	2.54	,HIS401,GLU398,TRP349,
			TRP349:CA--O:Lig	3.25	
	Cambogic acid	-11.7	SER511:HN--O:Lig	2.04	TYR510, PHE40
			ARG514:HH21--O:Lig	2.87	
	Dihydromorelloflavone	-11	ASN277:OD1--H:Lig	2.55	ARG273, GLU145, HIS345, LYS363
			ARG518:HH11--O:Lig	2.16	ASP367, PHE274, HIS374, PRO346
			HIS374----H:Lig	2.47	
	Luteolin 7-glucuronide	-10.4	Arg514:OE2--H:Lig	2.76	GLU375, PHE274 ,PRO346
			LYS363:HZ2--O:Lig	2.34	
	Morelloflavone	-11	Nil		ARG273, HIS345, LYS363,GLU145
					ASP367, PHE274, HIS374, PRO346
	Oxyguttiferone K	-10.4	ARG273:OE2-H:Lig	2.26	PHE274, CYS344, ALA153
			A:HIS345:CE1--O:Lig	3.54	TRP271, PRO346, CYS344
			ARG518:HH11--O:Lig	2.71	
	Rheediaxanthone A	-10.3	GLY143:HN--O:Lig	1.91	PHE274, ALA153

			HIS163:HE2--O:Lig	2.57	

Supplementary Table 3: Interaction details of hit molecules with M^{pro}

Target protein	Phytochemicals	Binding energy(Kcal/mol)	Hydrogen bond	Bond length(A^0)	Hydrophobic interaction
Mpro	1,4-Dicaffeoylquinic acid	-7.7	CYS44:O-H:Lig	2.76, 2.30	MET165, PRO168
			CYS44:O-H:Lig	431.00	
			LEU141:O--H:Lig	2.54	
			SER144:OG--H:Lig	2.35	
	Amentoflavone	-9.2	SER144:OG--O:Lig	3.29	HIS41,MET49,CYS145
			CYS145:SG--O:Lig	3.47	,MET165,
			GLU166:OE1--H:Lig	2.62	GLU166, PRO168,
			ARG188:O--H:Lig	2.69	
			GLN192:NE2--O:Lig	2.67	
			GLN192:O--H:Lig	2.83	
			HIS41:O--H:Lig	2.50	
			CYS44:O--H:Lig	2.36	
	Cambogic acid	-7.7	THR25:HG1--O:Lig	2.29	HIS41, MET165, MET49
			HIS41:HD1--O:Lig	2.67	
			GLY143:HN--O:Lig	2.48	
			HIS41:CE1--O:Lig	3.31	
			ASN277:OD1--H:Lig	2.55	
	Dihydromorelloflavone	-8.3	ARG518:HH11--O:Lig	2.16	PHE274, PRO346
			HIS374--H:Lig	2.47	
			THR26:O--H:Lig	2.37	
			ARG188:O--H:Lig	2.37	

	Luteolin 7-glucuronide	-7.9	GLN189:OE1--H:Lig	2.70	MET165
			THR26:HN--O:Lig	1.82	HIS41
			THR26:HE21--O:Lig	2.39	
			ARG188:O--H:Lig	2.19	
			GLN189:OE1--H:Lig	2.80	
	Morelloflavone	-8.5	LEU141:O--H:Lig	2.82	MET165
			SER144:OG--H:Lig	1.93	
			GLY143:HN--O:Lig	2.62	
			SER144:HG--O:Lig	2.78	
			ASN142:HD21--O:Lig	2.62	
	Oxyguttiferone K	-7.5	ARG105:HH21 --O:Lig	2.79	MET165, LEU167, PRO168, MET48
					HIS41, HIS163
	Rheediaxanthone A	-7.6	ARG349:HH22--O:Lig	2.38	CYS85, VAL186, PHE134, PHE181

Supplementary Table 4: Interaction details of hit molecules with RdRp

Target protein	**Phytochemicals**	**Binding energy(Kcal/mol)**	**Hydrogen bond**	**Bond length(A^0)**	**Hydrophobic interaction**
RdRp	1,4-Dicaffeoylquinic acid	-8.7	SER397:HG--O:Lig	2.62	PRO461, ARG349
			ASP390:O-H:Lig	2.07	
			LEU388:O-H:Lig	2.34	
			LEU389:CA--O:Lig	3.75	
			SER397:HN - N:Lig	2.84	
			SER318:CB--O:Lig	3.34	
			THR319:CA--O:Lig	3.53	

	Amentoflavone	-9.9	GLU350:OE1--H:Lig	1.87	VAL315,PRO323,
			THR394:CB--O:Lig	3.62	ARG349,PRO461,PRO677
			ARG569:HE --O:Lig	2.28	
			ARG569:HE --O:Lig	2.40	
	Cambogic acid	-7.2	THR687:HN --O:Lig	2.49	LYS500, ALA512, ALA685
			ALA688:HN--O:Lig	2.02	
			TYR689:HH --O:Lig	1.91	
			PRO677:O--H:Lig	2.97	
			VAL315:O--H:Lig	2.33	
	Dihydromorelloflavone	-9.5	THR394:O--H:Lig	2.52	LEU460, PRO461, PRO677, ARG349
			SER318:CB--O:Lig	3.54	PRO323
			SER814:OG--H:Lig	2.83	
			GLU811:OE2--H:Lig	2.56	
	Luteolin 7-glucuronide	-8.6	TRP617:O--H:Lig	2.28	LYS798, PRO620
			ASP618:OD1--H:Lig	2.04	
			ASP760:O--H:Lig	2.28	
			PHE793:O--H:Lig	2.40	
			LYS551:HZ3 --O:Lig	2.05	
			SER795:HN --O:Lig	2.32	
			PRO677:O--H:Lig	2.36	
			PRO461:CD--O:Lig	3.79	
	Morelloflavone	-9.2	ARG249:HE - N:Lig	2.64	LEU460, PRO461, ARG349, ARG249
			ASN496:HN ---O:Lig	2.33	
			ARG569:HH21--O:Lig	2.89	
	Oxyguttiferone K	-7.7	LYS577:HZ1--O:Lig	2.11	LYS500, ALA685, VAL557, VAL560
			ILE494:O--H:Lig	1.94	
			ASN497:HN - -O:Lig	2.49	
	Rheediaxanthone A	-8.2	ARG33:NH2 - --O:Lig	3.25	ARG569,VAL560, LEU576, TYR689, LYS500

Supplementary Table 5: Interaction details of hit molecules with NFkB

Target protein	Phytochemicals	Binding energy(Kcal/mol)	Hydrogen bond	Bond length(A^0)	Hydrophobic interaction
NFκB	1,4-Dicaffeoylquinic acid	-7.5	SER45:OG - --O:Lig	2.97	PRO275, LYS56
			SER45:OG - --O:Lig	2.70	
			GLU225:OE1--H:Lig	2.83	
			GLU225:OE2--H:Lig	2.69	
			SER45:O--H:Lig	2.11	
			GLY31:CA - --O:Lig	3.46	
			SER51:CB - --O:Lig	3.55	
			THR52:OG1--N:Lig	4.00	
			LYS221:O--H:Lig	2.11	
	Amentoflavone	-9.6	GLU222:O--H:Lig	2.75	LYS28,ARG50,ASP223,PHE239,PRO275
			GLU22:OE1--H:Lig	2.45	
			LEU179:N --O:Lig	3.08	
	Cambogic acid	-8.6	TYR254:OH --O:Lig	3.13	TYR20, GLY270, GLN271, MET279
			GLU225:OE2-H:Lig	2.70	
			SER45:O--H:Lig	2.81	
	Dihydromorelloflavone	-9.5	GLY31:CA-O:Lig	3.33	MET279
			GLU49:OE1-H:Lig	2.75	
			GLY31:O--H:Lig	2.25	
	Luteolin 7-glucuronide	-8.8	GLN29:N --O:Lig	2.90	LYS28, SER276, PRO275, SER276
			GLN29:NE2 --O:Lig	3.22	
			ASP53:N - --O:Lig	2.81	
			GLU49:O--C:Lig	3.42	

			GLU49:O-C:Lig	3.46	
			GLU49:O-C:Lig	3.52	
			ILE224:O--H:Lig	2.28	
			GLN241:NE2 - N:Lig	3.42	
	Morelloflavone	-8.9	THR52:OG1 - --O:Lig	3.18	LYS28, PHE239
			ASP223:OD1-H:Lig	2.96	
	Oxyguttiferone K	-8.3	THR52:CA - --O:Lig	3.35	LYS28, ARG50, GLU225, PRO275,
	Rheediaxanthone A	-9	SER45:O--H:Lig	2.11	LYS28, ARG236, PHE239, PRO275
			THR52:O--H:Lig	2.77	
			ASP53:CA -O:Lig	3.52	